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2018-06

Vohlonen , I J , Hakama , M , Harkonen , M , Malila , N , Pukkala , E , Koistinen , V & Sipponen , P 2018 , ' Oesophageal cancer incidence in 20-year follow-up in a population-based sample of 12 000 middle-age men with or without *Helicobacter pylori* infection in Finland ' , Gut , vol. 67 , no. 6 , pp. 1201-1202 . <https://doi.org/10.1136/gutjnl-2017-314913>

<http://hdl.handle.net/10138/236593>

<https://doi.org/10.1136/gutjnl-2017-314913>

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Oesophageal cancer incidence in 20-year follow-up in a population-based sample of 12 000 middle-age men with or without *Helicobacter pylori* infection in Finland

Two consensus reports on *Helicobacter pylori* (Hp), published recently in *Gut*, summarise the role of Hp gastritis in upper GI diseases, including gastric cancer (GCA).^{1,2} Although Hp gastritis definitely increases the risk of GCA as suggested in both reports, Hp is, on the other hand, also associated with a notable low incidence of oesophageal cancer (EC), of both adenomatous and squamous type.

In our earlier 15-year follow-up of a large population-based sample of males aged 50–65 years (n=12 016) from two Finnish cities, with or without Hp, diagnosed in 1994–1996 by serological (IgG) Hp test (Biohit HealthCare, Helsinki, Finland), 57 GCA cases were recorded in

the study population by the nationwide Cancer Registry during the follow-up.³ Of these cancers, 50 were in men and seven in those with and without Hp, respectively. The relative standardised incidence ratio (RR) of GCA incidence in Hp positive compared with that in Hp-negative men, calculated with the Altman's procedure, was 6.0 (95%CI 2.3 to 19.0).

In a 20-year follow-up of the same population sample, 39 ECs appeared during the follow-up. Of these, 29 were in the Hp-negative subgroup (6625 men) and 10 in the Hp-positive subgroup (5391 men) (table 1). Of the cancers in Hp-negative and in Hp-positive subgroups, 11 and three were ECs of adenocarcinoma type and 14 and six of squamous cell type, respectively. In five cases, the histological type was unknown. All estimates of RR of EC in the Hp-positive men compared with EC in the Hp-negative men were very low, as shown in table 1, indicating that the Hp gastritis associates strongly with reduced EC risk. In addition to ECs of adenocarcinoma type also, the RR of squamous cell EC was notably low (table 1). Serum level of pepsinogen I did not markedly alter any of the RR estimates.

The prevented fraction of EC due to Hp positivity was very high, 78%. In comparison, the corresponding attributable percentage of GCA in Hp-positive men was 84%.³ Thus, relatively, the Hp gastritis reduces EC incidence roughly similarly as it increases GCA incidence. However, the incidence rate of GCA in the present study population was nearly twice as high as the incidence of EC. Therefore, the numbers of GCA caused by Hp positivity were nearly twice the numbers of EC prevented by Hp positivity.

Lower than the expected risk of oesophageal cancer in men with Hp gastritis has been presented in several other studies (see, eg, Nie *et al*, Rokkas *et al*, Islami and

Kamangar, Xie *et al*, Ye *et al*, de Martel *et al*, Whiteman *et al*^{4–10}). The reason of this low risk is unknown. So far, the most plausible explanation is the intragastric acidity that tends to be lower in patients with Hp gastritis than in those without it. In people with 'healthy' stomach, a highly acid gastro-oesophageal refluxate, in persons prone and liable to GERD, may promote cascades that result in acid-related erosive and finally cancerous lesions in the oesophageal epithelium. In this context, in contrast to alkaline reflux, the acid reflux into the oesophagus is likely the key factor that associates with the increased risk and incidence of EC.

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Correction notice This article has been corrected since it published Online First. The CI in the second paragraph has been updated to 6.0 (95% CI 2.3 to 19.0).

Contributors All authors have had a specific task in the processing of the study. IJV, as a team leader, was in charge of design and preparatory writing. MH was in charge of selecting the statistical procedures. MHN was in charge of implementing the laboratory tests. NM was in charge of analysing qualitatively the cancer register. EP was in charge of statistical analyses of cancer register. VK was in charge of calculating the RRs and the corresponding 95% CIs. PS was in charge of qualitative assessment of differences between cardiac and oesophageal cancers.

Table 1 Numbers and relative standardised incidence ratios (RR and 95% CI) of oesophageal cancer in *Helicobacter pylori* (Hp) antibody (HpAb) positive and negative middle-age men from two cities followed up by National Cancer Registry in Finland from 1994 to 1996 to 2014

	Hp status		Risk ratio (RR)	95% CI of RR
	Hp positive (≥30 HpAb (IgG) enzyme immunoassay unit)	Hp negative (<30 HpAb (IgG) enzyme immunoassay unit)		
Number of men	6625 (6178) *	5391 (5232)*		
Number of person years	107 714 (100 810)*	89 961 (87 461)*		
Number of cancers in follow-up by type of cancer				
Adenomatous	3	11	0.22	0.05 to 0.95
Squamous	6	14	0.35	0.12 to 1.01
Other or unknown	1	4	–	–
Total	10 (7)*	29 (28)*	0.28	0.13 to 0.60

*Numbers in brackets give the respective number of cases after excluding the men with atrophic gastritis (serum pepsinogen I <25 µg/L).

Competing interests MH and PS are members of the Scientific Committee and shareholders of Biohit Oyj, a company which develops and markets laboratory tests, including biomarker tests for gastrointestinal diseases. MHN is a Board Member of the company. There are no other conflicts of interest.

Ethics approval The National Ombudsman of Finland, the National Institute of Health and Welfare and the Ethical Committee of the University Hospital of Eastern Finland.

Provenance and peer review Not commissioned; internally peer reviewed.



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To cite Vohlonen IJ, Hakama M, Härkönen M, *et al.* *Gut* 2018;**67**:1201–1202.

Received 25 July 2017

Revised 15 August 2017

Accepted 20 August 2017

Published Online First 31 August 2017

Gut 2018;**67**:1201–1202.

doi:10.1136/gutjnl-2017-314913

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